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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/535,667

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Hiromi Imamura

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EXAMINER

GUDIBANDE, SATYANARAYAN R

ART UNIT

PAPER NUMBER

1654

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/535,667	<b>Applicant(s)</b> IMAMURA ET AL.	
	<b>Examiner</b> SATYANARAYANA R. GUDIBANDE	<b>Art Unit</b> 1654	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 11-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☒ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>8/24/05, 5/19/05</u> . | 6) <input type="checkbox"/> Other: ____.  |

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## **DETAILED ACTION**

### ***Election/Restrictions***

No election/restriction was made in the instant application as the claims as presented exhibited unity of invention.

Claims 11-22 are pending.

Claims 11-22 are examined on the merit.

### ***Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(a)-(d) as follows:

Perfecting a claim to priority under 35 U.S.C. 119(a)-(d) within the time period set in 37 CFR 1.55(a)(1) or filing a grantable petition under 37 CFR 1.55(c). See MPEP § 201.13. The foreign priority filing date must antedate the reference and be perfected. The filing date of the priority document is not perfected unless applicant has filed a certified priority document in the application (**and an English language translation, if the document is not in English**) (see 37 CFR 1.55(a)(3)) and the examiner has established that the priority document satisfies the enablement and description requirements of 35 U.S.C. 112, first paragraph. Hence priority to the foreign application JAPAN 2002-337212 filed 11/20/2002 is denied.

### ***Information Disclosure Statement***

The information disclosure statement filed 5/19/05 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

### ***Claim Objections***

Claim 21 is objected to because of the following informalities: The letter “T” is missing from the first word “The” on line 1. Appropriate correction is required.

Claim 11 is objected to because of the following informalities: The claim reads on lines 4-6 as “A subunits have at least one substitution of Ala residue for the 232<sup>nd</sup> Ser **and** Ser residue for the 235<sup>th</sup> Thr residue”. It appears that applicants meant “A subunits have at least one substitution of Ala residue for the 232<sup>nd</sup> Ser **or** Ser residue for the 235<sup>th</sup> Thr residue”. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 101***

#### **35 U.S.C. 101 reads as follows:**

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

**Claims 11-22** are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant claims are asserted to be useful for a nanoactuator of a micromachine or a

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nanomachine or the like (page 1, lines 10-11). The instant specification also discloses that for fabrication of a micro- or a nano machine development of various technologies is required (page 1, lines 22-24). However, no such technologies or nature of the aforementioned various technologies are apparent from the instant disclosure. Thus, in the instant case, the utility is a 'general utility' (*see MPEP § 2107.01(I)*), “[I]ndicating that a compound may be useful in treating unspecified disorders, or that the compound has "useful biological" properties, would not be sufficient to define a specific utility for the compound. Similarly, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target”; “A general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.”).

Further, the MPEP states that the following categories are not substantial utilities: (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved; (B) A method of treating an unspecified disease or condition; (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility; (D) A method of making a material that itself has no specific, substantial, and credible utility; and (E) A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility. *MPEP § 2107.01(I)*.

Further, with regards to research tools, the MPEP states, “An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted

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utility requires further research to identify or reasonably confirm. Labels such as "research tool," "intermediate" or "for research purposes" are not helpful in determining if an applicant has identified a specific and substantial utility for the invention." MPEP § 2107.01(I).

Additionally, the art recognizes no specific or substantial utility for the compound(s) of the invention. For example, a nano or a micro-machine of molecular size comprising a molecular complex similar to the one claimed in the instant application is known or available to assess the aspect of credible or substantial utility in the instant case.

### ***Claim Rejections - 35 USC § 112***

**The following is a quotation of the first paragraph of 35 U.S.C. 112:**

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claims 11-22** are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 11-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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In the instant invention, applicants claim a heat resistant rotary molecule V1-ATpase a complex derived from *Thermus Thermophilus* having three A subunits, three subunits and one D subunit wherein A subunits have at least one substitution of Ala residue for Ser at position 232 and Ser for the Thr at position 235 in SEQ ID NO:3.

The instant invention as recited, claims a heat resistant rotary molecule. However, the nature of interactions between subunits and the order in which the 3 subunits of A, 3 subunits of B and 1 subunit of D in the complex is not apparent from the claims as recited and the from the disclosure as originally filed in the application. The art discussed by Imamura, et al., 2003, PNAS, 100, 2312-2315 clearly identifies the complex of the subunit and its attachment to the substrate and also identifies the mutations in the form of substitutions in various subunits.

The MPEP clearly states that the purpose of the written description is to ensure that the inventor had possession of invention as of the filing date of the application, of the subject matter later claimed by him. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997). The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the application. These include, "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art

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to the conclusion that the applicant was in possession of the claimed invention is sufficient”

MPEP 2163.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

Claim 11 as recited does not provide a complete composition of the rotary motor complex. Figure 1., of the specification depicts a schematic diagram of the rotary molecule complex. However, all the elements of the figure are not recited in claims as presented. The nature of association between the different polypeptide subunits and the order in which the subunits are arranged in the complex is neither recited in the claims nor disclosed in the specification.



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Claim 12 recites a limitation “substrate” the claim as recited or the specification as disclosed do not adequately define the nature of this substrate, with the exception that figure 1 depicts Ni-NTA coated glass.

Claims 14-16 recites a limitation “joint material”. The term “joint material” has been given a broad definition in the specification as the ‘material for transmitting rotational motion of the D subunit of the V1-ATpase to another component e.g., a gear or shaft of a motion engine or the like”. The specification also explicitly excludes that this joint material is “not for connection to another component” (page 13, lines 1-2). It is also disclosed as plurality of beads and a fine fiber such as actin filament. The claim as recited does not indicate the nature of association between the joint material and the V1-ATpase complex. The specification as disclosed does not adequately support the invention as claimed in the instant invention. The claim as recited also lacks a SEQ ID NO., for subunit B which forms the part of the complex.

Therefore, the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 17-19 recites the limitation " at least one of Cys residue substituted for the 48th Glu residue and Cys residue substituted for the 55th Gin residue in SEQ ID NO: 5" in lines 2-3. There is insufficient antecedent basis for this limitation in the base claim 11.

Claim 20-22 recites the limitation " all Cys residues in the A subunit and the B subunit are replaced by non-Cys residues" in lines 1-2. There is insufficient antecedent basis for this limitation in the base claim 11.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 11-22 rejected under 35 U.S.C. 102(a) as being anticipated by Imamura, et al., 2003, PNAS, 100, 2312-2315.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

In the instant invention, applicants claim a heat resistant rotary molecule V1-ATpase a complex derived from thermus thermophilus having three A subunits, three subunits and one D

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subunit wherein A subunits have at least one substitution of Ala residue for Ser at position 232 and Ser for the Thr at position 235 in SEQ ID NO: 3.

The reference of Imamura teaches the instant invention wherein the V1-ATpase is derived from thermus thermophilus (Abstract). The reference teaches that the rotary molecule V1-ATpase composed of A3B3D1F1 subunits (page 2312, column 1, paragraph 2). The reference teaches the S232A and T235S mutations in subunit A, His-8-tags in subunit A; and E48C and Q55C mutations in subunit D (page 2312, column 2, paragraph 1). This reads on instant claims 11 and 17-19. The figure 1 on page 2313 discloses that V1-ATpase was attached to glass surface (substrate) via His-tag of A subunits. This reads on instant claim 12 and 13. The figure 1 also reveals that a bead was attached through subunit D and hence reads on instant claims 14-16, wherein the beads corresponds to joint material according the instant specification (page 13, lines 5-6). The reference also discloses that the 9 Cysteine residues of A and B subunits were substituted with Serine residues to ensure specificity of newly introduced Cysteine residues in subunit D with the biotin-maleimide reagent (page 2313, column 2, paragraph 1). This meets the limitations of instant claims 20-22. Hence the cited reference of Imamura anticipates the instant invention.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yokoyama, 2000, The Journal of biological chemistry, 275, 13955-13961 in view of Xiong, 1995, The Journal of biological chemistry, 270, 23300-23304.

In the instant invention, applicants claim a heat resistant rotary molecule V1-ATpase a complex derived from thermus thermophilus having three A subunits, three subunits and one D subunit wherein A subunits have at least one substitution of Ala residue for Ser at position 232 and Ser for the Thr at position 235 in SEQ ID NO: 3.

The reference of Yokoyama discloses the A, B, D and F subunits of V1-ATpase (abstract) and further discloses that V1 has been proposed to have a central shaft subunit that rotates in the A3B3 hexagon (page 13955, column 2, paragraph1) this reads on claim 11 of instant invention. The disclosure of the subunit A teaches the SEQ ID NO:3 of the instant invention.

However, the Yokoyama reference does not teach A subunits to have at least one substitution of Ala residue for Ser at position 232 and Ser for the Thr at position 235 in SEQ ID NO: 3.

The reference of Xiong teaches alanine scanning mutagenesis of  $\epsilon$  subunit of F1-F0 ATP synthetase. The reference teaches that 19 amino acids were changed to alanine either singly or in pairs between residues 10 and 93 of  $\epsilon$  subunit of F1-F0 ATP synthetase. The study indicated that mutations fell into two groups, the first group had inhibited ATPase activity and the second group had stimulated ATPase activity (Abstract). One of ordinary skill in the art would infer from this study that alanine scanning alters the function of polypeptides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Yokoyama and Xiong to arrive at the instant invention to alter the function of A subunit of V1-ATPase as taught by Xiong. The skilled artisan would have been motivated to do so given the fact that Alanine scanning is a well known method to alter the function of the polypeptide as taught by Xiong. There would have been a reasonable expectation of success, given the fact that Xiong, et al., were successful in showing that substitution of various residues in the  $\epsilon$  subunit of F1-F0 ATP synthetase by Ala residue altered the function of polypeptide to impart desired function.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the

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references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R Gudibande/  
Examiner, Art Unit 1654

/Andrew D Kosar/  
Primary Examiner, Art Unit 1654